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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,367	02/26/2004	Michael Graupe	USAV2001/0143 US CNT	7957

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EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/787,367	GRAUPE ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12,13 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-9,13 and 15* is/are allowed.

6)☒ Claim(s) *10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-10, 12-13, and 15 are currently pending in the instant application.

2. Firstly, to prevent any confusion, the Examiner notes that Applicants have mistakenly referred to the instant application as serial number 10/767,367 in the Amendment, while the correct serial number is actually 10/787,387.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority based on application PCT/US02/29323. It is noted, however, that applicant has not filed a certified copy of the PCT application as required by 35 U.S.C. 119(b).

Response to Amendment

4. Receipt is acknowledged of Applicants' Amendment and Reply, filed January 17, 2006, which has been entered of record in the file. Accordingly, claims 11, 14, and 16 have been cancelled, and claims 1, 4, 7, 8, 12, 13, and 15 have been amended.

Claim Rejections - 35 USC § 112

5. Claims 11 and 12 previously rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 11 has been cancelled, rendering said rejection moot.

(b) Claim 12 previously rejected under 35 U.S.C. 112, because the sequence of steps (D)-(J) was confusing. Applicants have amended claim 12 such that steps (B)-(H) are independent of each other and are each optional. However, step (F) is still confusing because it is unclear from the claim language whether Applicants are intending to resolve any type of

isomer of the instant compounds (which includes many compounds not found in the specification), or the **stereoisomers** of compounds of Formula (I), as discussed on page 43 of the specification. The Examiner warns that as the claim reads now, it encompasses all types of isomers of the instant compounds, which Applicants are not enabled for. Applicants can overcome this rejection by replacing every occurance of "isomer" in step (F) with the term "stereoisomer."

In step (G), the Examiner notes that the word "acceptable" has been omitted after "pharmaceutically" and before "prodrug."

6. Claims 10 and 11 previously rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. While various diseases/disorders may be listed in the specification, the claims are not enabled for *all* disorders responsive to the inhibition of Cathepsin S, since the claims give no indication as to the full range of disorders that could be treated/prevented using the instant claimed method. Since Applicants have cancelled claim 11, the pending enablement rejection is only applicable to claim 10.

Applicants traverse the rejection, arguing that one skilled in the art would be able to make and sue the preset inventions without engaging in undue experimentation. The Examiner respectfully disagrees, since as previously stated, Applicants are only enabled for a number of diseases that are treated by administering a compound that inhibits the Cathepsin S pathway. However, Applicants are not enabled for all diseases that are encompassed *by the language* of claim 10.

The claim is drafted in terms of inhibiting the pathway of Cathepsin S, which in turn might allegedly prevent, inhibit, or ameliorate the pathology and/or symptomology of certain

disesases, but is not a specific utility such that one skilled in the art would know how to perform the claimed method for treating a specific disease or diseases of real world relevance.

The nature of the claimed invention in Claim 10 is a "method of use" claim for inhibiting Cathepsin S, along with one step of the method to accomplish this ("administering to the animal a therapeutically effective amount of compound of Claim 1...").

Regarding the breadth of the claims, the applicable rule is that "Each claim must be separately analyzed and given its broadesetr reasonable interpretation in light of and consistent with the written description." MPEP 2163 (II)(I), citing In re Morris, 127 F. 3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). Applying this rule to Claim 10, the broadest reasonable interpretation of the claim would encompass a method of inhibiting the pathway of Cathepsin S. According to the Specification, the scope of diseases which would be affected by inhibition of Cathepsin S would include autoimmune disorders (which include juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris, Grave's disease, myasthenia gravis, systemic lupus erythemotasus, rheumatoid arthritis and Hashimoto's thyroiditis, all of which there is no known cure and certainly no known prevention), allergic disorders (asthma, etc), allogenic imune responses (organ transplant rejections or tissue grafts, etc), COPD, bronchiolitis, excessive airway elastolysis, pneumonities, and cardiovascular disease (e.g. plaque rupture and atheroma), please see the Specification pages 34-35.

Regarding the predictability in the art, even though Cathepsin S pathways have been identified as one of the five main targets for drug development, as a practical matter their use as therapeutic agents for "preventing" the pathology of autoimmune disorders, or for "treating" a broad range of types of diseases, remains unpredictable.

Applicants have not demonstrated that inhibiting the biochemical pathway of Cathepsin S and treating or preventing the pathology of the many diseases/ disorders described in the specification and encompassed by claim 10 are inexorably linked. The efficacy of an individual compound against a specific disease or symptom needs to be specifically and individually supported by factual evidence. The specification also only discusses a few basic compounds in four *in vitro* assays which describe their inhibition constants on pages 70-72, and provide no data for describing the efficacy of the claimed compounds for treating the full scope of disorders that the language of claim 10 encompasses. Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the art would be burdened with undue "experimentation study" to determine whether the claimed compounds not only inhibit the activity of a chemokine, but also treat disorders of real-world relevance.

Given the literature references cited (using similar inhibitors), the known art at the time, the high skill level of practitioners of the art, along with the *in vitro* data for the claimed invention and information about preferred dose and route of administration, a person of skill in the art would not require an undue quantity of experimentation to be enabled to use the claimed invention as a method for inhibiting Cathepsin S for treating certain certain specific disorders/diseases. On the other hand, the disclosure does not provide sufficient data for the claimed invention to be used by the skilled artisan as "a method of treating a disease...in which inhibition of Cathepsin S can prevent, inhibit, or ameliorate the pathology and/or symptomology of the disease," without an undue quantity of experimentation when those limitations are given their full range of interpretation beyond the scope of the specific diseases mentioned on pages 34-35 of the specification, as well as those discussed in the journal articles including specific

bone resorption disorders, specific lung disorders, etc.

In sum, the Specification provides very little direction or guidance to enable a person of ordinary skill in the art to use the claimed invention for the treatment or prevention of all diseases encompassed by the language of claim 10, even where limited to specific diseases (autoimmune disorders). However, for "treating" certain specific diseases, the Specification and journal articles do provide direction and guidance to enable one of ordinary skill in the art to administer compounds of Formula (1) to "animals" by various forms and dose ranges, as described on page 35 of the Specification.

Again, the Examiner suggests claiming the possible diseases and conditions that are treated, rather than claiming the mechanism, which is speculative, and recommends the following language, "A method of inhibiting Cathepsin S, for treating asthma, COPD, and bronchiolitis, etc (to name a few)... comprising administering to an animal in need thereof, a therapeutically effective amount of a compound of Claim 1...."

Conclusion

7. Claims 1-10, 12-13, and 15 are pending in the application, claims 10 and 12 stand rejected, and claims 1-9, 13, and 15 appear allowable over the prior art.

8. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
April 10, 2006

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

Joseph K. M°Kane
SPE, Art Unit 1626